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ANALYSIS BY NASA'S VESGEN SOFTWARE OF RETINAL BLOOD VESSELS IN HUMAN SUBJECTS UNDERGOING HEAD-DOWN TILT DURING 70-DAY BED REST

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INTRODUCTION AND BACKGROUND

Significant risks for visual impairment associated with increased intracranial pressure (VIIP) are incurred by microgravity spaceflight, especially long-duration missions [1]. We hypothesize that microgravity-induced fluid shifts result in pathological changes within blood vessels of the retina that precede development of visual and other ocular impairments. Potential contributions of retinal vascular remodeling to VIIP etiology are therefore being investigated for two studies in 30° infrared (IR) Heidelberg Spectralis® images with NASA's innovative VESsel GENeration Analysis (VESGEN) software [2,3]. The retrospective studies include: (1) before, during and after (pre, mid and post) 6º head-down tilt (HDT) in human subjects during 70 days of bed rest, and (2) before and after missions to the International Space Station (ISS) by U.S. crew members. Results for both studies are almost complete. A preliminary example for HDT is described below.

METHODS

The mature (beta-level), automated VESGEN software was developed as a translational and basic vascular research discovery tool to map and quantify branching vascular patterns, particularly for retinal vascular disease [2-4]. IR Spectralis® images of retinal blood vessels from the retinas of six healthy human subjects undergoing HDT were collected by NASA previously [5]. For our 2013 NASA NRA award, VESGEN analysis of the IR images was approved by NASA's Institutional Review Board (Pro1384) according to previously published methods for progressive, visually impairing vascular disease in the human retina [2,3]. In brief, binary vascular patterns are extracted from grayscale images, and automatically analyzed by VESGEN according to weighted physiological branching rules. For Phase 1, the initial portion of our study, the pre, mid and post bed rest status of retinal images was blinded to the VESGEN analysts. Longitudinal status of the images will be revealed during Phase 2, when final VESGEN results will be correlated with other ophthalmic and medical findings such as visual acuity, changes in retinal thickness and optic nerve, and cardiovascular parameters such as blood pressure.

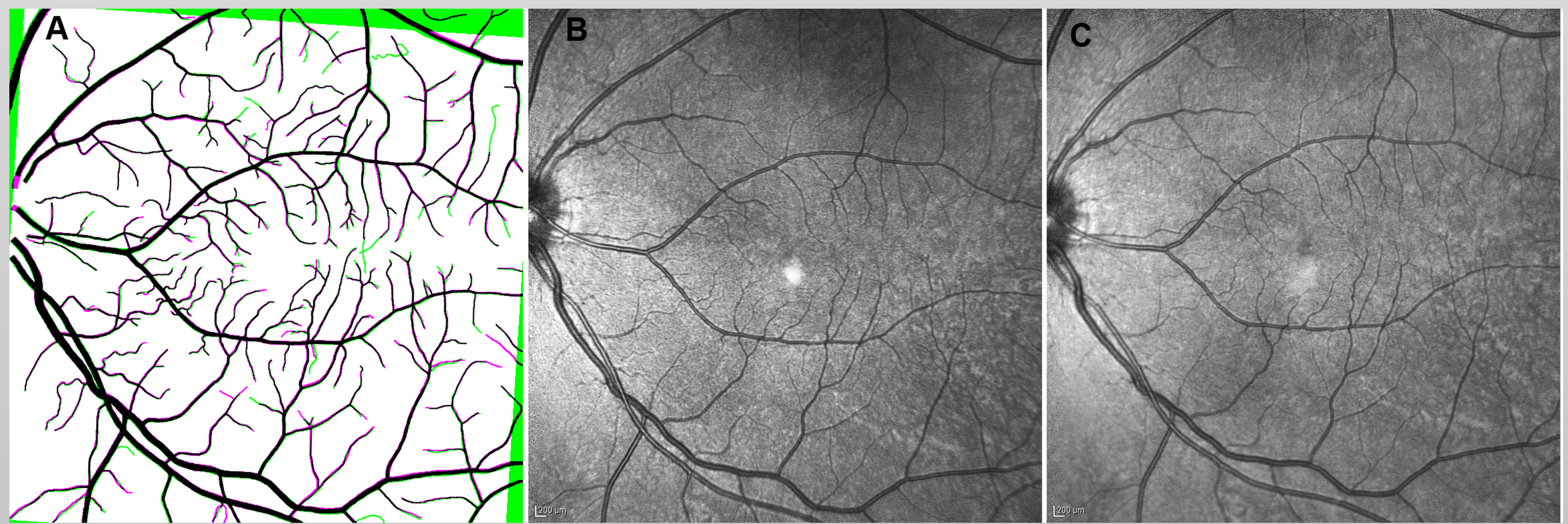

Figure 1 Comparison of two images of an HDT retina using a masking transformation by Matlab® algorithm

(A) Pink vessels correspond to vessels from Image 1 (reference), Green vessels correspond to Image 2 (transformed to fit reference). Both interpretations are in agreement where the vessels appear black, whereas, the pink and green vessels show vessel differences. (B,C) Grayscale Images 1 and 2.

The smaller blood vessels, which in general remodel most actively during progression of vascular-dependent diseases, are not easily resolved from image background by the low-resolution (low contrast) IR Spectralis® imaging modality (average resolution for HDT images, 11.4 micron/pixel). Therefore a novel tool was developed with Matlab® (Mathworks) for aligning vessels in pre, mid and post images (Figure 1) to compare (query) differences in image capture of critically important small vessels.

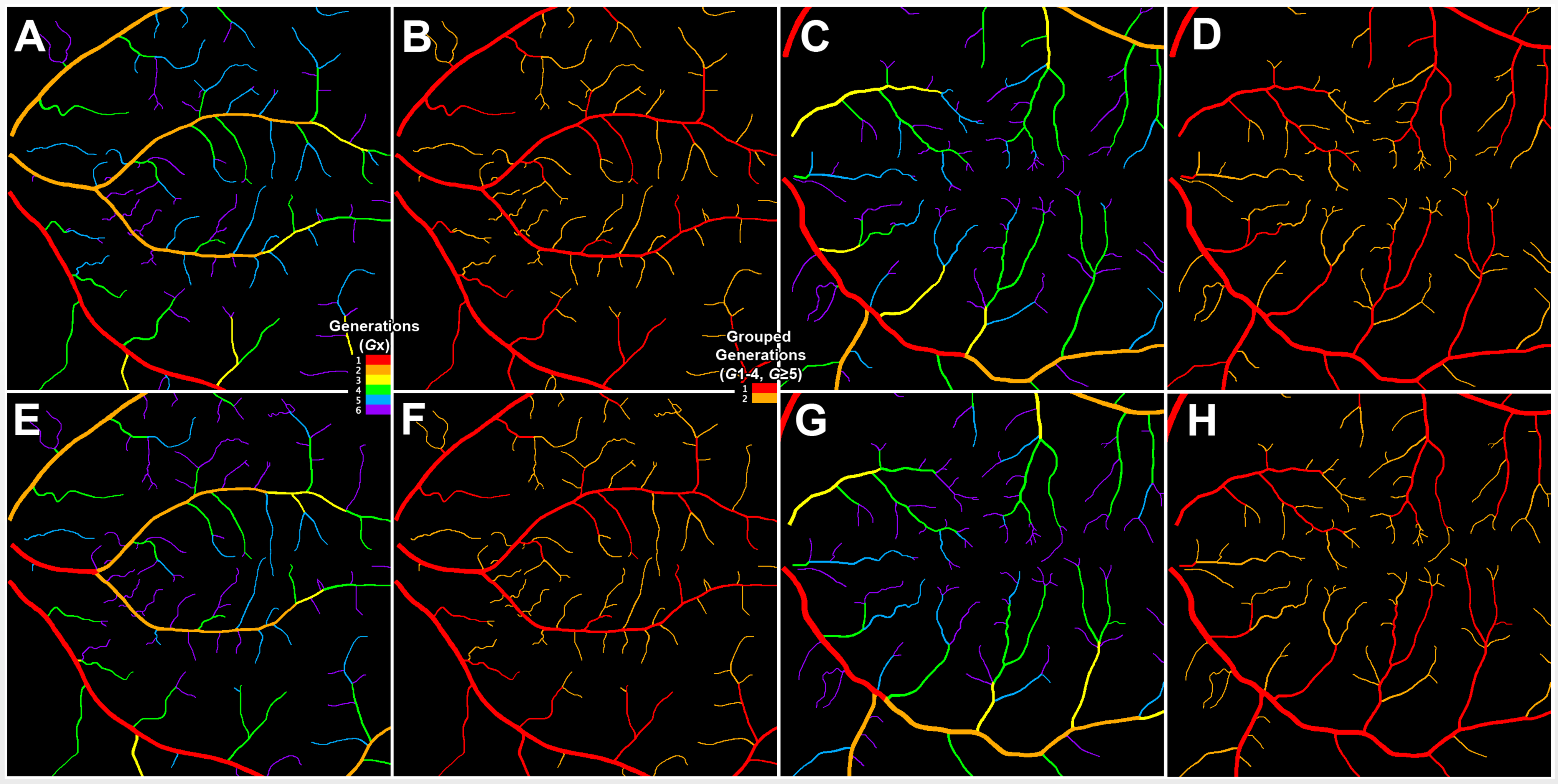

Figure 2 Arterial and venous branching generations within 2 images of an HDT retina currently blinded as to pre and post status

(A–D) Image 1 arterial generations, arterial generations grouped, venous generations and venous generations grouped. (E–H) Image 2 arterial and venous generations. (B,F,D,H) Vessels were grouped into generations of $G_{1\text{-}4}$ and $G_{\geq 5}$.

RESULTS AND DISCUSSION

The VESGEN analysis of HDT images (Phase 1) is complete. However, because the Phase 1 VESGEN analysis of Crew Members is not yet finished, the pre, mid and post status of HDT images remains blinded. Two images of the same HDT retina are therefore presented as an example of the VESGEN analysis (Figure 2). For the grouped Images 1 and 2, the number of large and small vessels ($N_{1\text{-}4}$ and $N_{\geq 5}$) are 34 and 83 compared to 33 and 83 for arteries (C,F), and 37 and 92 compared to 33 and 102 for veins (D,H). Space-filling capacities of the arterial and venous branching trees were quite consistent by space-filling measures such as vessel length density (L_v) and the fractal dimension (D_f). For arteries (C,F), L_v and D_f were 1.41E-3 and 1.45E-3 μm/μm^2, and 1.37 and 1.38, compared to 1.40E-3 and 1.44E-3 μm/μm^2, and 1.33 and 1.33, for veins (D,H). Arterial and venous diameters of grouped large and small vessels were quite equivalent.

CONCLUSIONS

The study is scheduled to conclude in mid April 2017. Preliminary inspection of the Spectralis® images, supported by VESGEN analysis, suggest that the IR images lack sufficient resolution to definitively test our hypothesis, which proposes that small blood vessels within the retina remodel to accommodate and mediate prolonged cephalad fluid shifts. Newer ophthalmic imaging such as OCT angiography (OCT-A) and adaptive optics scanning laser ophthalmoscopy (AOSLO) offer significant advances in retinal vascular resolution that, combined with VESGEN analysis, would provide the necessary imaging technology to conclusively test the hypothesis.

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